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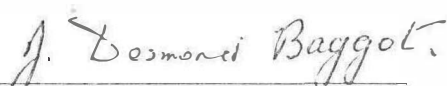
**PHARMACOKINETICS OF IMIDOCARB IN NORMAL AND FEBRILE  
DOGS AND GOATS**

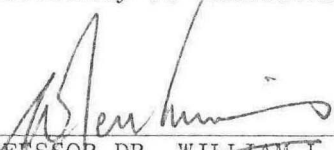
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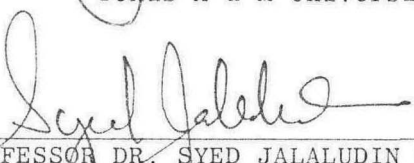
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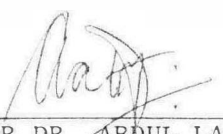
This thesis attached hereto, entitled "Pharmacokinetics of Imidocarb in Normal and Febrile Dogs and Goats" prepared and submitted by Abdul Salam Abdullah in partial fulfilment of the requirements for the degree of Doctor of Philosophy, is hereby accepted.

  
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PHARMACOKINETICS OF IMIDOCARB IN NORMAL  
AND FEBRILE DOGS AND GOATS

by

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A Thesis

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## ABSTRACT

Disposition kinetics of imidocarb, an antiprotozoan drug, was studied in normal and febrile dogs and goats. Fever was induced using E. coli endotoxin, Trypanosoma evansi and Infectious Bovine Rhinotracheitis (IBR) virus. The objectives of the study were to compare the disposition kinetics of imidocarb in ruminant and monogastric species, and the influence of fever of different etiology on the disposition kinetics of this drug. The concentration of imidocarb in body fluids and tissues were measured by spectrophotometry.

The disposition kinetics of imidocarb in normal and febrile dogs and goats can be adequately described by a two-compartment open model. The apparent volume of the central compartment,  $V_c$ , was significantly lower ( $P < 0.01$ ) but the volume of distribution,  $V_{d(\text{area})}$  was significantly higher ( $P < 0.05$ ) in normal goats than in dogs. Higher volume of distribution and the ratio of imidocarb level in peripheral-to-central compartment in goats (6:1) prolonged elimination of the drug, resulting in considerably higher levels of the drug still present in the tissues 14 days after a single subcutaneous or intramuscular dose. Thus the withdrawal time of imidocarb was estimated to be 5-6 weeks in this food-producing species. Differences in the kinetic disposition of imidocarb in dogs and goats may be largely attributed to the anatomical and physiological differences in the gastrointestinal tract between the two species.

The results of the present study indicate that fever of different etiologies affected the disposition kinetics of imidocarb

differently. Plasma concentrations of imidocarb were higher than normal during endotoxin-induced fever but lower during Trypanosoma-induced fever. Although concentrations of imidocarb in the plasma of goats were not affected by the IBR viral-induced fever, the apparent volume of distribution,  $V_{d(\text{area})}$ , and the steady-state volume of distribution,  $V_{d(\text{ss})}$ , were significantly lowered as in the endotoxin-induced fever. Similarly, the above kinetic parameters as well as volume of central compartment,  $V_c$ , and the body clearances  $Cl_B$  were significantly higher ( $P < 0.01$ ) in dogs and goats during Trypanosoma-induced fever than in the normal animals although the plasma concentrations were substantially reduced during the febrile reaction. The microconstants were also affected differently by fever of different etiology. Nevertheless, half-life of imidocarb remained unaffected during the three febrile conditions.

Therefore, it could be hypothesized that fever of different etiology affected the disposition kinetics of imidocarb differently and the influence of fever on pharmacokinetics should be considered beyond the plasma concentrations and half-life of the drug itself. Furthermore, the pathophysiology of the disease and not just the febrile state should be considered when evaluating the influence of disease conditions on the disposition kinetics of a drug.

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## TABLE OF CONTENTS

No.		Page
1.	TITLE PAGE .....	i
2.	ABSTRACT .....	ii
3.	ACKNOWLEDGEMENT .....	iv
4.	TABLE OF CONTENTS .....	v
5.	LIST OF TABLES .....	viii
6.	LIST OF FIGURES .....	xiv
7.	GENERAL INTRODUCTION .....	1
8.	LITERATURE REVIEW.....	5
8.1	Pharmacokinetics.....	5
8.1.1	Introduction.....	5
8.1.2	Principles of Pharmacokinetic Analysis .....	6
8.1.3	Pharmacokinetic parameters.....	12
8.1.3.1	Actual pharmacokinetic rate constants.....	12
8.1.3.2	Volume of distribution.....	14
8.1.3.3	Steady-state volume of distribution.....	18
8.1.3.4	Biologic Half-life.....	20
8.1.3.5	Body clearance.....	23
8.1.4	Drug distribution.....	25
8.1.5	Influence of disease on drug distribution.....	30
8.2	Fever .....	31
8.2.1	Introduction .....	31
8.2.2	Pathogenesis of fever.....	33
8.2.3	Pathophysiology of fever.....	34
8.3	Influence of fever on pharmacokinetics.....	36



## TABLE OF CONTENTS

No.		Page
8.4	Influence of fever on pharmacokinetic of drugs in domestic animals.....	39
9.	MATERIALS AND METHODS .....	41
9.1	Experimental Animals .....	41
9.2	Restraint of Animals .....	42
9.3	Drug and Chemicals .....	42
9.4	Fever Inducing Agents .....	44
9.4.1	Endotoxin .....	44
9.4.2	Viruses .....	44
9.4.3	<u>Trypanosoma evansi</u> .....	44
9.5	Induction of Fever .....	44
9.5.1	Using <u>E. coli</u> endotoxin .....	44
9.5.2	Using viruses .....	45
9.5.3	Using <u>Trypanosoma evansi</u> .....	46
9.6	Quantitation of Febrile Response .....	50
9.7	Sample Collection .....	52
9.8	Analytical Techniques .....	53
9.9	Preparation of Standards .....	55
9.10	Analysis of Data .....	65
10.	EXPERIMENTAL PROCEDURES .....	66
10.1	Pharmacokinetics of Imidocarb in normal dogs and goats .....	66
	Experiment 1: Intravenous injection of imidocarb dipropionate to normal dogs and goats .....	66
	Experiment 2: Subcutaneous and intramuscular injection of imidocarb dipropionate to normal dogs and goats.....	66



## TABLE OF CONTENTS

No.		Page
10.2	Pharmacokinetics of imidocarb in febrile dogs and goats .....	67
	Experiment 3: The influence of <u>E. coli</u> endotoxin-induced fever .....	67
	Experiment 4: The influence of <u>Trypanosoma evansi</u> -induced fever .....	68
	Experiment 5: The influence of IBR viral-induced fever in goats .....	68
11.	RESULTS .....	70
11.1	Normal Dogs and Goats .....	70
	Experiment 1: Intravenous administration of imidocarb dipropionate to normal dogs and goats .....	70
	Experiment 2: Subcutaneous and intramuscular administration of imidocarb dipropionate to normal dogs and goats.....	83
11.2	Febrile Dogs and Goats .....	101
	Experiment 3: The influence of <u>E. coli</u> endotoxin-induced fever.....	101
	Experiment 4: The influence of <u>Trypanosoma</u> -induced fever .....	115
	Experiment 5: The influence of IBR viral-induced fever .....	128
12.	DISCUSSION.....	136
13.	SUMMARY OF CONCLUSIONS .....	154
14.	REFERENCES .....	156



## LIST OF TABLES

No.		Page
I.	Methods for calculating volume of distribution when disposition kinetics of drug are described by two-compartment open model	16
II.	Absorbance for different fluids and tissues at a single concentration (15 µg/ml or gm)	64
III.	The mean $\pm$ SD observed (measured) concentration of imidocarb in the plasma of dogs (n=7) and goats (n=8) given a single intravenous dose (4 mg/kg) of imidocarb dipropionate	71
IV.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in normal dogs (n=7) following intravenous injection of a single dose (4 mg/kg) of imidocarb dipropionate solution	74
V.	Pharmacokinetic parameters (mean $\pm$ SD) describing disposition kinetics of imidocarb in normal goats (n=8) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	75
VI.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in normal dogs (n=7) and normal goats (n=8) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	79

# LIST OF TABLES

No.		Page
VII.	Comparison of two-and three-compartment models using mean concentration-time data (13 points) in normal goats (n=8)	82
VIII.	The mean $\pm$ SD observed (measured) plasma concentrations of imidocarb ( $\mu\text{g/ml}$ ) in normal dogs (n=7) and goats (n=4) following subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	84
IX.	The mean $\pm$ SD observed (measured) plasma concentrations of imidocarb ( $\mu\text{g/ml}$ ) in normal goats (n=4) following intramuscular injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	85
X.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in normal dogs (n=7) following subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	91
XI.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in normal goats (n=4) following subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	92

## LIST OF TABLES

NO.		Page
XII.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in normal goats (n=4) following intramuscular injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	93
XIII.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in normal dogs (n=7) and normal goats (n=4) following subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	94
XIV.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in normal goats following subcutaneous (n=4) and intramuscular (n=4) injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	95
XV.	The mean $\pm$ SD observed (measured) plasma concentration of imidocarb ( $\mu\text{g/ml}$ ) in normal and endotoxin-induced febrile dogs and goats following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	102

## LIST OF TABLES

No.		Page
XVI.	Pharmacokinetic parameters describing kinetics of imidocarb in febrile (endotoxin-induced fever) dogs (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	107
XVII.	Pharmacokinetic parameters describing disposition kinetics of imidocarb in febrile (endotoxin-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	108
XVIII.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in the normal (n=7) and febrile (endotoxin-induced fever) dogs (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	109
XIX.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in the normal (n=8) and febrile (endotoxin-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	110



## LIST OF TABLES

No.		Page
XX.	The mean $\pm$ SD observed (measured) plasma concentrations of imidocarb ( $\mu\text{g/ml}$ ) in normal and Trypanosoma-induced febrile dogs and goats following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	116
XXI.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in the febrile (Trypanosoma-induced fever) dogs (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	121
XXII.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in the normal (n=7) and febrile (Trypanosomiasis) dogs (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	122
XXIII.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in the febrile (Trypanosoma-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	123



## LIST OF TABLES

No.		Page
XXIV.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetics of imidocarb in the normal (n=8) and febrile (Trypanosoma-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	124
XXV.	The mean $\pm$ SD observed (measured) plasma concentrations of imidocarb ( $\mu$ g/ml) in normal (n=8) and febrile (IBR viral-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution	129
XXVI.	Pharmacokinetic parameters describing the disposition kinetics of imidocarb in the febrile (IBR viral-induced fever) goats (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb solution	132
XXVII.	Pharmacokinetic parameters (mean $\pm$ SD) describing the disposition kinetic of imidocarb in the normal (n=8) and febrile (IBR-viral induced fever) goats (n=6) following intravenous injection of a single dose (4mg/kg) of 12% imidocarb dipropionate solution	133



## LIST OF FIGURES

No.		Page
1.	<p>Infectious disease system. In the course of an infectious disease and continuous antibiotic treatment the body of the host (H), the microbes (M) and the antibacterial drug (D) are the interdependent variables of a complex system. The interactions in the system are: 1: Pharmacokinetics (<math>H \longrightarrow D</math>), 2: Drug toxicity (<math>D \longrightarrow H</math>), 3: Host's defense mechanisms (<math>H \longrightarrow M</math>), 4: Bacterial toxicity (<math>M \longrightarrow H</math>), 5: Pharmacodynamics (<math>D \longrightarrow M</math>), 6: Bacterial defense mechanisms (<math>M \longrightarrow D</math>). (From Hinderling, 1978. Significance of the pharmacokinetics of antimicrobial drugs. Scand. J. Infect. Dis. Suppl. 14:25-35).</p>	2
2	<p>Schematic diagram of the two-compartment open model. The dose of drug is introduced into the central compartment, where it distributes instantaneously. Distribution between central and peripheral compartments takes place more slowly; <math>k_{12}</math> and <math>k_{21}</math> are first-order rate constants for drug transfer between the two compartments. Elimination, which comprises biotransformation and excretion, is assumed to occur exclusively from the central compartment; <math>k_{e1}</math> is the</p>	8





## LIST OF FIGURES

No.		Page
2	first-order rate constant for drug elimination from the central compartment. (From Baggot, 1978. Some aspects of clinical pharmacokinetics in veterinary medicine. I. J. Vet. Pharmacol. Therap. 1, 5-18).	8
3.	Semilogarithmic graph depicting the time course of drug in the plasma after intravenous administration of a single dose. The equation which describes the disposition curve is shown. (From Baggot, 1977). Principles of Drug Disposition in Domestic Animals: The Basis of Veterinary Clinical Pharmacology. Saunders, Philadelphia. □ Residual ● Experimental.	10
4.	Analogue computer-generated curves showing kanamycin levels (as fraction of intravenous dose) in the central and peripheral compartments and the cumulative amount excreted in the urine as a function of time. The curves are based on microconstants which were derived from experimental pharmacokinetic constants obtained in sheep. (From Baggot, 1978. Some aspects of clinical pharmacokinetics in veterinary medicine I. J. Vet. Pharmacol. Therap. 1, 5-18).	17



## LIST OF FIGURES

No.		Page
5.	Graphical technique for estimating the half-life of a drug. (From Baggot, 1977. Principles of Drug Disposition in Domestic Animals: The Basis of Veterinary Clinical Pharmacology. Saunders, Philadelphia).  $B = 10 \mu\text{g/ml}; t_{\frac{1}{2}} = 1.5 \text{ h.}$	21
6.	Schematic representation of the distribution of drugs into different compartments. (From Klotz 1976. Pathophysiological and Disease-induced Changes in Drug Distribution Volume: Pharmacokinetic Implications. Clinical Pharmacokinetics 1:204-218).	29
7.	Postulated pathway for the pathogenesis of fever. Endogenous pyrogen circulates to the hypothalamus (PO/AH), where it induces the production of a metabolite of arachidonic acid. This substance, in turn, increases the synthesis of norepinephrine, an alpha-adrenergic agonist that increase the production of cAMP. This cyclonucleotide then directly causes alterations in the activity of temperature-sensitive neurons that bring about an increase in heat conservation or production	35



# LIST OF FIGURES

No.		Page
7.	(or both). Ag = antigen; Ag-Ab=antigen-antibody complexes; Compl = complement; cAMP = cyclic 3', 5'-adenosine monophosphate; DHS = delayed hypersensitivity; EP = endogenous pyrogen; 5HT = serotonin; LK = lymphokine; NE = norepinephrine; PO/AH = preoptic area of anterior hypothalamus; RES = reticulo-endothelial system $\Rightarrow$ inhibitors; $\Rightarrow$ activators. (From Bernheim HA, Block LH, Atkins E: Fever: Pathogenesis, pathophysiology, and purpose. Ann Intern Med 91:261, 1979).	35
8.	A dog and goat in restraining cages	43
9.	Mean febrile response of dogs ( $\star \longrightarrow \star$ ) and goats ( $\bullet \longrightarrow \bullet$ ) following intravenous injection of LPS <u>E. coli</u> (0.2 $\mu$ g/kg) (first arrow) and after the injection of imidocarb dipropionate (second arrow) in relation to time. Each point represents the mean of six dogs and six goats.	47
10.	Mean febrile response of dogs ( $\star \longrightarrow \star$ ) and goats ( $\bullet \longrightarrow \bullet$ ) following intravenous inoculation of $10^7$ <u>Trypanosoma evansi</u> and after the injection of imidocarb dipropionate (arrow) in relation to time. Each point represents the average of six dogs and goats.	48



## LIST OF FIGURES

No.		Page
11.	Mean febrile response of goats following intravenous inoculation of Infectious Bovine Rhinotracheitis (IBR) Virus (first arrow) and after the injection of imidocarb dipropionate (second arrow) in relation to time. Each point represents the mean of six goats.	49
12.	Standard curve of imidocarb in plasma of goat.	56
13.	Standard curve of imidocarb in urine of goat.	57
14.	Imidocarb standard curve in bile	58
15.	Imidocarb standard curve in kidney	59
16.	Imidocarb standard curve in liver	60
17.	Imidocarb standard curve in heart	61
18.	Imidocarb standard curve in muscle	62
19.	Imidocarb standard curve in fat	63
20.	The least squares non-linear regression line which best describes the plasma concentration-time profile in normal dogs. Data used for	72



## LIST OF FIGURES

No.		Page
20.	construction of graph represents the mean $\pm$ SD concentration-time data in dogs (n=7).	72
21.	The least squares non-linear regression line which best describes the plasma concentration-time profile in normal goats. Data used for construction of graph represents the mean $\pm$ SD concentration-time data in goats (n=8).	73
22.	Computer generated curves, based on micro-constants associated with the two-compartment open model showing the level of imidocarb in compartments of the two-compartment open model. The fraction of dose in each of the compartments at 8-hours after a single intravenous injection (4 mg/kg) in dog is: 6.3% (central), 14.1% (peripheral), and 79.6% (eliminated). The concentrations in plasma are shown.	77
23.	Computer generated curves, based on micro-constants associated with the two-compartment open model showing the level of imidocarb in compartments of the two-compartment open model. The fraction of dose in each of the compartments at 8-hours after a single	78



## LIST OF FIGURES

No.		Page
23.	intravenous injection (4 mg/kg) in goats is: 2.8% (central), 18.9% (peripheral), and 78.3% (eliminated). The concentrations in plasma are shown.	78
24.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in the normal dogs (n=7) and goats (n=8) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	81
25.	Semilogarithmic plot of the plasma concentration-time profiles for imidocarb which followed injection of the drug (4 mg/kg) in dogs by the intravenous and subcutaneous (n=7) routes. The symbols represent the concentration of imidocarb in the plasma after the administration of a single intravenous dose (●—●) and a single subcutaneous dose (★—★).	86
26.	Semilogarithmic plot of the plasma concentration-time profiles for imidocarb which followed injection of the drug (4mg/kg) in goats by the intravenous (n=8), subcutaneous (n=4) and intramuscular (n=4) routes. The symbols	87

## LIST OF FIGURES

No.		Page
26.	represent the concentration of imidocarb in the plasma after the administration of a single intravenous dose (●—●), subcutaneous dose (★—★) and intramuscular dose (□—□).	87
27.	Concentration of imidocarb ( $\mu\text{g/ml}$ ) in plasma of normal dogs ( $n=7$ ) and goats ( $n=4$ ) following subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	89
28.	Concentration of imidocarb ( $\mu\text{g/ml}$ ) in plasma of normal goats following subcutaneous ( $n=4$ ) and intramuscular ( $n=4$ ) injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	90
29.	Concentration of imidocarb in various tissues of normal goats following subcutaneous and intramuscular injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	97
30.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in normal goats following intravenous ( $n=8$ ) and intramuscular ( $n=4$ )	98

## LIST OF FIGURES

No.		Page
30.	injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	98
31.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in normal goats following intravenous (n=8) and subcutaneous (n=4) injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	99
32.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in normal dogs (n=7) following intravenous and subcutaneous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	100
33.	The least squares non-linear regression line which best describes the plasma concentration-time profile in endotoxin-induced febrile dogs. Data used for construction of graph represents the mean $\pm$ SD concentration-time data in febrile dogs (n=6).	103
34.	The least squares non-linear regression line which best describes the plasma concentration-time profile in endotoxin-induced febrile goats. Data used for construction of graph represents the mean $\pm$ SD concentration-time data in febrile goats (n=6).	104





## LIST OF FIGURES

No.		Page
35.	The least squares non-linear regression lines which best describes the plasma concentration-time profile in normal and endotoxin-induced febrile dogs. Data used for construction of graphs represents the mean $\pm$ SD concentration-time data in normal (n=6) and febrile dogs (n=6).	105
36.	The least squares non-linear regression lines which best describe the plasma concentration-time profiles in normal and endotoxin-induced febrile goats. Data used for construction of graphs represents the mean $\pm$ SD concentration-time data in normal (n=8) and febrile goats (n=6).	106
37.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in the normal (n=7) and febrile (endotoxin-induced fever) dogs (n=6) following intravenous injection of a single dose (4 mg/kg) of 12% imidocarb dipropionate solution.	113
38.	Cumulative urinary excretion (mean + SD) of unchanged imidocarb in the normal (n=8) and febrile (Endotoxin-induced fever) goats (n=6)	114